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Safety and efficacy of Amoklor (ammonium chloride) as a zootechnical additive for ruminants, cats and dogs

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)

Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of Amoklor (ammonium chloride) as a zootechnical additive for ruminants, cats and dogs. A concentration of 10,000 mg Amoklor/kg complete feed is considered as safe for ruminants when administered during a restricted feeding period (< 3 months). For longer periods of administration, a concentration of 5,000 mg Amoklor/kg is considered safe. For cats, 5,000 mg Amoklor/kg in the complete diet can be considered safe for an unlimited period. Data for dogs are limited to three short-term studies with small numbers of animals. The adverse effect seen in one study would suggest that the dose for dogs should be limited to 5,000 mg Amoklor/kg. As both ions of ammonium chloride will be rapidly excreted predominantly via the kidney, no increase in the endogenous concentration of these ions in tissues and products is expected. The use of Amoklor in animal nutrition does not raise any concerns for consumer safety. Amoklor should be considered as an irritant to skin, eyes, the digestive and respiratory tract, and a dermal and respiratory sensitiser. The use of Amoklor in feedingstuffs at the maximum level of 10,000 mg/kg does not pose a risk for the environment. Supplementation with 10,000 mg Amoklor/kg feed for ruminants reduces urinary pH and the formation of urinary calculi, and is efficacious on the prevention of milk fever (hypocalcaemia) at early lactation in old high-yielding dairy cows. Supplementation of feed for cats and dogs with 5,000 mg Amoklor/kg results in a decrease in urinary pH and is expected to protect against the formation of urinary calculi.

Keywords: zootechnical additive, Amoklor, safety, efficacy, ruminants, cats, dogs

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7.

The European Commission (EC) received a request from Latochema Co Ltd[2] for authorisation of the product Amoklor (ammonium chloride), when used as a feed additive for ruminants, pigs, cats and dogs (category: zootechnical additives; functional group: other zootechnical additives). During the assessment, the applicant requested a change to the designated target species excluding pigs. Therefore, the current application for authorisation is for ruminants, cats and dogs.[3]

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 26 November 2014.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product Amoklor (ammonium chloride), when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

Amoklor is a feed additive based on the active substance ammonium chloride. Ammonium chloride is authorised as a zootechnical additive, functional group other zootechnical additives, for lambs for fattening[4] and for ruminants, cats and dogs.[5]

Commission Directive 2008/38/EC7 on animal feedingstuffs for particular nutritional purposes lists under essential nutritional characteristics the 'urine-acidifying properties'. This characteristic is applicable to feed intended for the reduction of the risk of renal calculi and milk fever (hypocalcaemia) in ruminants including pregnant cows and dissolution or reduction of the occurrence of struvite stones in animals. One substance that has been used routinely to generate these effects is ammonium chloride.

Ammonium chloride is listed as a pharmacologically active substance in veterinary medicinal products and is not subject to maximum residue levels when used in food-producing animals (Commission Regulation (EC) No 37/2010).[6]

EFSA has issued two opinions on the safety and efficacy of ammonium chloride as feed additives (EFSA FEEDAP Panel, 2012a,b) and two other opinions on the safety of ammonium chloride used with foodstuffs (EFSA, 2009; EFSA CEF Panel, 2011).

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Latochema Co Ltd. R. Fereou 2 & G. Digeni, 3091 Limassol, Cyprus.
[3] Technical dossier/Supplementary information October 2015 /Annex 4.
[4] Commission implementing regulation (EU) No 832/2012 of 17 September 2012 concerning the authorisation of a preparation of ammonium chloride as a feed additive for lambs for fattening (holder of authorisation Latochema Co. Ltd) OJ L 251, 18.9.2012, p.27.
[5] Commission implementing regulation (EU) No 725/2013 of 26 July 2013 concerning the authorisation of ammonium chloride as a feed additive for ruminants, cats and dogs (holder of the authorisation BASF SE) OJ L 202, 27.7.2013, p. 17.
[6] Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. OJ L15, 20.1.2010, p. 1

2. Data and Methodologies

2.1. Data

This assessment is based on data submitted by the applicant in the form of a technical dossier[7] in support of the authorisation request for the use of Amoklor (ammonium chloride) as a feed additive. The technical dossier was prepared following the provisions of Article 7 of Regulation (EC) No 1831/2003 and the applicable EFSA guidance documents.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, to deliver this output.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[8]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Amoklor (ammonium chloride) is in line with the principles laid down in Regulation (EC) No 429/2008[9] and the relevant guidance documents: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012c), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011a), Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008, revised in 2009), Guidance for establishing the safety of additives for the consumer (EFSA FEEDAP Panel, 2012d), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012e) and Guidance on the assessment of additives intended to be used in pets and other non-food-producing animals (EFSA FEEDAP Panel, 2011b, revised in 2012).

3. Assessment

3.1. Characterisation

3.1.1. Characterisation of the product

Ammonium chloride is produced by chemical synthesis from ammonia and sodium chloride in water. After the reaction, ammonium chloride is separated by crystallisation and dried. As ammonium chloride is hygroscopic, 1% of tricalcium phosphate or trisodium phosphate is added as anticaking agent.

The active substance ammonium chloride (NH_4Cl, Chemical Abstracts Service (CAS) number 12125-02-9, molecular weight 53.5 g/mol; melting point: 350°C; density: 1.519 g/cm^3) is a solid crystalline powder and contains (before the addition of anticaking agent) by specification a minimum of 99.5% (three batches: 99.55–99.63%)[10] of ammonium chloride. The maximum specified sodium chloride content is 0.5%; the average concentration was 0.39%.

The specifications of the applicant for heavy metals analysed by atomic absorption spectrometry (AAS) were < 5 mg/kg expressed as lead and 3 mg/kg for iron. Both specifications were confirmed in three batches. Sulphate content was < 0.02% and the pH (200 g ammonium chloride/L solution, 25°C) varied between 5.15 and 5.20.[11] No dioxins and dioxins-related PCB were found in three batches.[12] Tricalcium phosphate (1.2%) was added after analysis.

[7] FEED dossier reference: FAD-2014-0033.
[8] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/default/files/FinRep-FAD-2010-0242%2B0037.pdf
[9] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.
[10] Technical dossier/Section II/Annex II 2;_Annex II 3; Annex II 4.
[11] Technical dossier/Section II/Annex II 2;_Annex II 3; Annex II 4.
[12] Technical dossier/Section II/Annex II 10

The particle size distribution of six batches, as analysed by laser diffraction, showed an average percentage of 5.8% of particles less than 150 µm in diameter (range: 4.8–7.3%).[13] The dusting potential measured by the Stauber–Heubach method (average of three batches) was 0.44 g/m^3.[14]

3.1.2. Stability and homogeneity

The applicant claimed a shelf life of 2 years under ambient conditions but no data supporting the statement were provided.

The stability of the additive was studied in a feed for ruminants and a feed for cats. Each feed was prepared in mash and pelleted forms (together four samples) and stored for 3 months. The initial content of ammonium chloride was 10,000 mg/kg (1%) and the analysed percentage of chloride in the dry matter before storage ranged between 0.73 and 0.76% in the four batches. The feed was stored under ambient conditions without control of the temperature and humidity. At the end of the storage period, the percentage of chloride in the dry matter ranged between 0.71 and 0.75%. The pelleting process (temperature of pelleting 70°C) in the two feed types did not cause a decrease in the average content of chloride.[15]

The homogeneity of the additive was tested in a concentrate feed (one batch, 10 subsamples) containing 30% barley, 20% wheat 15% corn, 32% co-products and some additives (3%) in a pilot paddle mixer (Type Buehler). The inclusion rate was 0.5% and the percentage of Amoklor was determined by the analysis of chloride. Total recovery of Amoklor was 103% with a coefficient of variation of 4.9%.[16]

3.1.3. Conditions of use

Amoklor is intended for use in feeds for ruminants, cats and dogs at an inclusion level of 10,000 mg/kg feedingstuffs for a period not exceeding 3 months. If the additive is administered for a period exceeding 3 months the inclusion level of 5,000 mg/kg feedingstuffs is proposed without limitation on the administration period.[17]

3.2. Safety

3.2.1. Safety for the target species

No specific studies with the additive under application were submitted. Instead, the applicant provided a literature review, which summarises studies in ruminants, cats and dogs. Although none of the studies reviewed could be described as a tolerance study, they allow conclusions to be drawn on the ammonium chloride level that is safe for ruminants, cats and dogs. More details are described in EFSA FEEDAP Panel (2012a,b).

Safety for ruminants

Ammonium chloride is a non-protein nitrogenous (NPN) substrate extensively used in ruminant feeding. It is a potential soluble N-source, usable by the rumen bacteria for their own protein synthesis and it may contribute to meet the protein requirements of ruminants. A concentration of 50 mg ammonia/L of rumen fluid is considered as optimal for microbial protein synthesis (Satter and Slyter, 1974). Undesirable effects in ruminants result from a too fast and/or a too abrupt release of ammonia. Sufficient energy easily fermentable in the rumen (e.g. carbohydrates from cereals), a thorough mixing with the ration, and a spread of diet intake over time are the most important protective factors.

Cattle

The acidifying capacity of ammonium chloride following the dietary-cation-anion-difference (DCAD) concept (Suttle, 2010), and the activation of the calcium metabolism in pregnant ruminants by a mild

[13] Technical dossier/Section II/Annex II 9 particle size.pdf.
[14] Technical dossier/Supplementary information October 2015/1.dusting potential analysis.pdf
[15] Technical dossier/Supplementary information October 2015/2.stability_testing_of_ammonium_chloride_in_feed.pdf
[16] Technical dossier/Section II/Annex II 1 homogeneity of ammonium chloride.pdf.
[17] Technical dossier/Supplementary information October 2015/3.proposed conditions of use.pdf

metabolic acidosis is also used to prevent milk fever (hypocalcaemia) occurrence in dairy cows after parturition, as demonstrated in some feeding studies (e.g. Block, 1984; Oetzel et al., 1988; Mellau et al., 2002; Goff et al., 2004; Goff, 2008). In such cases, ammonium chloride is given for 10–14 days before parturition until calving. Calcium absorption from the digestive tract and mobilisation from the bones of animals will be increased under these conditions (e.g. Gaynor et al., 1989; Block, 1994; Moore et al., 2000; Charbonneau et al., 2006).

Crookshank et al. (1973) evaluated ammonia toxicity in 466 feedlot cattle of mixed breeds, supplementing the diet with ammonium chloride at 10,000 mg/kg feed during 112 days. The authors concluded that ammonium chloride may be used as a source of non-protein nitrogen without clinical signs of ammonia toxicity up to 10,000 mg/kg of total ration.

Other studies in cows (Wang and Beede, 1992; Goff et al., 2004; Gelfert et al., 2009) included fewer animals (up to 11) and shorter feeding periods (up to 28 days) with ammonium chloride at 10,000 or 18,000 mg/kg feed. The results of these studies showed that supplemented cows had a lower blood pH, higher ionised calcium in blood and a greater urinary excretion of calcium than control cows. In some cases, the treatment induced a mild metabolic acidosis.

Castañeda et al. (2009) replaced gradually in five Holstein cows in a 5 × 5 Latin square 0.8% urea for 4 weeks each by ammonium chloride and did not observe any negative effect, however the design of the study does not allow further conclusions to be drawn.

Oetzel et al. (1988, 1991) also evaluated the toxicity of ammonium chloride at a lower level (5,000 mg/kg feed) in cows (up to 48) after a short administration period (up to 21 days). No signs of toxicity were reported in any of the studies considered, but urinary calcium excretion was increased.

Lambs

The effect of supplementation with ammonium chloride on urinary pH was evaluated by Bushman et al. (1967; 1968). In the first study, 72 Hampshire lambs were supplemented with 0, 5,000 and 15,000 mg ammonium chloride/kg feed in the diet for 84 days ad libitum. In the second study, 72 crossbreed lambs were supplemented with 10,000 mg ammonium chloride/kg feed in the diet for 88 days ad libitum. In both studies, supplementation with 10,000 or 15,000 mg ammonium chloride/kg feed significantly reduced urinary pH values and the incidence of urinary calculi. Serum calcium and phosphorus were not affected by the treatment in the first study, but serum magnesium was significantly reduced (from 2.73 to 2.37 and 2.33 mg/100 mL). Renal excretion of phosphorus and magnesium was not affected by the treatments, but calcium excretion significantly increased in both studies.

Similarly, Barlet et al. (1973) found in two studies with 12 or 15 lambs per group (0 or 10,000 mg ammonium chloride/kg feed for 35 days) a numerical reduction on the incidence of urolithiasis and a higher urinary excretion of calcium and phosphorus when supplementing the diet with ammonium chloride. Similar results were found by Crookshank (1970) with 5,000 mg ammonium chloride/kg supplemented to 40 wool lambs for 112 days.

Goats

The effect of diet supplementation with 20,000 mg ammonium chloride/kg on the urinary pH of goats was evaluated by Horst and Jorgensen (1974). Reduction in urinary and blood pH and an increase in urinary calcium and magnesium excretion were observed.

Jones et al. (2009) did not find adverse health effects, but a reduction in blood pH when ammonium chloride up to 14,700 mg/kg was supplemented in the diet of 24 goats for 7 days with a reduction in urinary pH. The authors concluded that supplementation with 6,800 mg ammonium chloride/kg was adequate to a DCAD of 0 mEq/kg feed and could be considered as a target for diet formulation in the prevention of urolithiasis.

The supplementation of complete feed for ruminants with ammonium chloride effectively decreases urinary pH and the formation or urinary calculi, increases the renal excretion of calcium and magnesium and may result in a mild metabolic acidosis. The acid–base balance (anion–cation ratio) of the diets may influence the effectiveness of the ammonium chloride supplementation. Therefore, considering the above-mentioned results and the variety of feedingstuffs with different anion–cation

ratios in the diet, the recommended dose of 10,000 mg ammonium chloride/kg complete feed can be considered safe for ruminants for a restricted feeding period (< 3 months).

For longer administration periods, which are not normally used in ruminant nutrition (mostly only about 10–14 days for milk fever prevention; see above), a dose of 5,000 mg ammonium chloride/kg complete feed is considered safe for ruminants.

Safety for cats and dogs

Ammonium chloride is used in the treatment and prevention of the feline urological syndrome. This is a multifactorial disorder characterised by difficulties or increased frequency of urination, blood or crystals in the urine and/or urethral obstruction. Urinary pH > 6.4 is considered to be one of the reasons for feline urological syndrome. Some studies demonstrated that ammonium chloride is an efficacious urinary acidifier in the management of feline urological syndrome.

Taton et al. (1984) fed 24 cats with dry commercial cat food with or without 15,000 mg ammonium chloride/kg food for 11 months. Ammonium chloride had no effect on food and water intake or body weight. Urinary pH remained constant throughout the study (7.0 for control and 5.9 with the ammonium chloride supplemented diet). Similar results for urinary pH are reported by Izquierdo and Czarnecki-Maulden (1991), but 22,000 mg ammonium chloride/kg food caused reduced feed intake. Ching et al. (1989; 1990) fed diets with 15,000 mg ammonium chloride/kg food for 6 months. The acidified diet was palatable, no significant differences in food intake and body weight were observed and urinary pH was decreased. The authors summarised that chronic dietary acidification with 15,000 mg ammonium chloride/kg food produced chronic metabolic acidosis and lower, or negative, calcium and potassium balance. The treatment did not produce significant changes in trabecular bone remodelling or bone mineral density in adult cats. Some authors (Ching et al., 1989; Kienzle and Wilms-Eilers, 1994; Kienzle et al., 1998) observed an increased renal magnesium excretion after ammonium chloride supplementation (500 mg ammonium chloride/kg body weight (bw) and day).

Some short-term studies (e.g. Börkü et al., 1996: 0, 50, 100, 200 and 400 mg ammonium chloride/kg bw per day for 30 days, five dogs per experimental group; Shaw, 1989: 200 mg ammonium chloride/kg bw to 11 dogs ranging in weight from 9 to 13 kg; Senior et al., 1984: 200 mg followed 100 mg ammonium chloride/kg bw per day for 14 days to four dogs weighing 14–18 kg) were reported. The authors describe a decrease in blood pH and severe adverse effects (e.g. diarrhoea) at approximately 10,000 mg ammonium chloride/kg food.

Supplementation with 10,000 mg ammonium chloride/kg food is well tolerated in cats. However, long-term supplementation produces chronic metabolic acidosis and lower, or negative, calcium and potassium balance. In addition, there are no data available to establish a safe administration period. Based on the available results, it is concluded that 5,000 mg ammonium chloride/kg in the complete diet can be considered safe in cats for an unlimited period.

For dogs, available data is limited to three short-term studies with small numbers of animals. Severe adverse effects (diarrhoea) seen in one study at a concentration of 10,000 mg ammonium chloride/kg food would suggest that the dose for dogs should also be limited to 5,000 mg/kg.

Conclusions on safety for the target species

A concentration of 10,000 mg Amoklor/kg complete feed is considered as safe for ruminants when administered during a restricted feeding period (< 3 months). For longer periods of administration, a concentration of 5,000 mg Amoklor/kg complete feed is considered safe.

For cats, 5,000 mg Amoklor/kg in the complete diet can be considered safe for an unlimited period.

Data for dogs are limited to three short-term studies with small numbers of animals. The adverse effects seen in one study would suggest that the dose for dogs should also be limited to 5,000 mg Amoklor/kg.

3.2.2. Safety for the consumer

In ruminants, ammonium chloride will dissociate in the rumen. The ammonia ion (NH_4^+) not used for microbial protein synthesis in the rumen will cross the rumen wall entering the liver via the blood

stream, where it is converted to urea. Urea can be recycled to the rumen across the ruminal epithelium or through saliva and used for microbial protein synthesis in the rumen or it can be rapidly excreted via the kidneys in urine (EFSA FEEDAP Panel, 2012a,b).

As both ions of ammonium chloride will be rapidly excreted predominantly via the kidneys, no increase in the endogenous concentration of these ions in tissues and products is expected. The use of Amoklor in animal nutrition does not therefore raise any concerns for consumer safety.

3.2.3. Safety for the user and the environment

Safety for the user and the environment were already assessed in the previous opinion on Amoklor (EFSA FEEDAP Panel, 2012a). The FEEDAP Panel considers that the proposed extension of use does not modify the conclusions reached in this assessment on safety for the user and safety for the environment.

Ammonium chloride should be considered as an irritant to skin, eyes, the digestive and respiratory tract, and a dermal and respiratory sensitiser.

The use of ammonium chloride in feedingstuffs at the maximum level of 10,000 mg/kg complete feed does not pose a risk for the environment.

3.3. Efficacy

The publications reviewed under Section 3.2.1 clearly indicate that ammonium chloride supplementation of feed for ruminants, cats and dogs results in a decrease in urinary pH.

As mentioned in the previous opinion on ammonium chloride (EFSA FEEDAP Panel, 2012b), 'The minimum effective dose in cattle to prevent urinary calculi is reportedly 2,000 mg/kg in a complete diet (Crookshank et al., 1973), and the lowest experimentally demonstrated dose to reduce urinary pH is 3,500 mg/kg (Castañeda et al., 2009). Experimental evidence for efficacy in reducing urinary pH for lambs is given at 10,000 mg/kg in the diet (Barlet et al., 1973; Bushman et al., 1968), and for goats it is 7,000 mg/kg in the diet (Jones et al., 2009)'. In addition, supplementation with 10,000 mg ammonium chloride/kg complete feed for ruminants reduces urinary pH and reduces the formation of urinary calculi; it is efficacious in the prevention of hypocalcaemia before parturition and milk fever in dairy cows (see 3.2.1).

The minimum dose that was effective in reducing urinary pH in cats was 4,000 mg/kg (Izquierdo and Czarnecki-Maulden, 1991), and it was approximately 6,000 mg/kg in dogs. It is expected that this decrease in urinary pH would be adequate to protect dogs and cats against the formation of urinary calculi. A pH value of about 6.5 is considered sufficient to dissolve urinary (struvite) calculi. A pH of 5.8–6.0 in urine is considered as a sign of chronic metabolic acidosis and negative calcium and potassium balance in cats (Ching et al., 1989).

The FEEDAP Panel concludes that supplementation with 10,000 mg Amoklor/kg complete feed for ruminants reduces urinary pH, reduces the formation of urinary calculi and is efficacious in the prevention of milk fever (hypocalcaemia) at early lactation in old high-yielding dairy cows.

The supplementation of feed for cats and dogs with 5,000 mg Amoklor/kg in the complete diet results in a decrease in urinary pH and is expected to protect against the formation of urinary calculi.

3.4. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[18] and Good Manufacturing Practice.

[18] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

4. Conclusions

A concentration of 10,000 mg Amoklor/kg complete feed is considered as safe for ruminants when administered during a restricted feeding period (< 3 months). For longer periods of administration, a concentration of 5,000 mg Amoklor/kg complete feed is considered safe.

For cats, 5,000 mg Amoklor/kg in the complete diet can be considered safe for an unlimited period.

Data for dogs are limited to three short-term studies with small numbers of animals. The adverse effect seen in one study would suggest that the dose for dogs should also be limited to 5,000 mg Amoklor/kg.

As both ions of ammonium chloride will be rapidly excreted predominantly via the kidneys, no increase in the endogenous concentration of these ions in tissues and products is expected. The use of Amoklor in animal nutrition does not therefore raise any concerns for consumer safety.

Amoklor should be considered as an irritant to skin, eyes, the digestive and respiratory tract, and a dermal and respiratory sensitiser.

The use of Amoklor in feedingstuffs at the maximum level of 10,000 mg/kg complete feed does not pose a risk for the environment.

The FEEDAP panel concludes that supplementation with 10,000 mg Amoklor/kg complete feed for ruminants reduces urinary pH, reduces the formation of urinary calculi and is efficacious on the prevention of milk fever (hypocalcaemia) at early lactation in old high-yielding dairy cows. The supplementation of feed for cats and dogs with 5,000 mg Amoklor/kg in the complete diet results in a decrease in urinary pH and is expected to protect against the formation of urinary calculi.

5. Recommendations

Added amounts of Amoklor should be considered in calculations of diets for ruminants to avoid higher nitrogen emissions.

Documentation provided to EFSA

1. Ammonium chloride (Amoklor). August 2014. Submitted by Latochema Co Ltd.
2. Ammonium chloride (Amoklor). Supplementary information. October 2015. Submitted by Latochema Co Ltd.
3. Comments from Member States.

References

Barlet JP, Theriez M, and Molenat, G, 1973. L`urolithiase ovine effets d`un phosphonate de sodium et du d´ammonium. Annales de Biologie Animale Biochimie Biophysique, 13, 627-641.

Block E, 1984. Manipulation of dietary anions and cations for prepartum dairy cows to reduce incidence of milk fever. Journal of Dairy Science 67: 2939-2948.

Block E, 1994. Manipulation of dietary cation-anion difference on nutritionally related production diseases, productivity, and metabolic responses of dairy cows. Journal of Dairy Science 77: 1437-1450.

Börkü MK, Kurtede A, Imren HY, Kalinbacak A, Tanyel B and Ilhan T, 1996. The effect of long term usage of ammonium chloride on some parameters in blood, urine and feces in dogs. Veterinary Journal of Ankara University 43: 235-246.

Bushman DH, Embry, LB and Emerick RJ, 1967. Efficacy of various chlorides and calcium carbonate in the prevention of urinary calculi. Journal of Animal Science, 26, 1199-1204.

Bushman DH, Emerick RJ and Embry LB, 1968. Effect of various chlorides and calcium carbonate on calcium, sodium, potassium and chloride phosphorus balance and their relationship to urinary calculi in lambs. Journal of Animal Science, 27, 490-496.

Charbonneau E, Pellerin D and Oetzel GR, 2006. Impact of lowering dietary cation-anion difference in nonlactating dairy cows: A meta-analysis. Journal of Dairy Science 89: 537-548.

Castaneda RD, Branco AF, Coneglian SM, Barreto JC, Granzotto F, Teixeira S, 2009. Replacing urea with ammonium chloride in cattle diets: digestibility, synthesis of microbial protein, and rumen and plasma parameters. Acta Scientiarium – Animal Sciences, 31, 271-277

Ching SV, Fettman MJ, Hamar DW, Nagode LA and Smith KR, 1989. The effect of chronic dietary acidification using ammonium chloride on acid-base and mineral metabolism in the adult cat. Journal of Nutrition 199: 902-915.

Ching SV, Norrdin RW, Fettman MJ and Lecouteur RA, 1990. Trabecular bone remodelling and bone mineral density in the adult cat during chronic dietary acidification with ammonium chloride. Journal of Bone and Mineral Research 5: 547-556.

Crookshank HR, 1970. Effect of ammonium salts on the production of ovine urinary calculi. Journal of Animal Science, 30, 1002–1004.

Crookshank HR, Smalley HE, Furr D and Ellis GFJr, 1973. Ammonium chloride and ammonium sulphate in cattle feedlot finishing rations. Journal of Animal Science 36: 1007-1009.

EFSA (European Food Safety Authority), 2008. Technical Guidance of the Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) for assessing the safety of feed additives for the environment. The EFSA Journal 2008, 842, 1–28.

EFSA (European Food Safety Authority), 2009. Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on Flavouring Group Evaluation 46 (FGE.46)1: Ammonia and two ammonium salts from chemical group 30. The EFSA Journal, 955, 1–34.

EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2011. Scientific opinion on Flavouring Group Evaluation 46, Revision 1 (FGE.46Rev1): Ammonia and three ammonium salts from chemical group 30. EFSA Journal, 9(2):1925, 35 pp.

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011a. Technical guidance: Tolerance and efficacy studies in target animals. EFSA Journal 2011;9(5):2175, 15 pp. doi:10.2903/j.efsa.2011.2175

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011b. Guidance on the assessment of additives intended to be used in pets and other non food-producing animals. EFSA Journal 2011;9(2):2012, 3 pp. doi:10.2903/j.efsa.2011.2012

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012a. Scientific opinion on ammonium chloride (Amoklor) for lambs for fattening. EFSA Journal, 10(2):2569, 11 pp.

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012b. Scientific Opinion on the safety and efficacy of ammonium chloride for bovines, sheep, dogs and cats. EFSA Journal 10(6):2738. 18 pp.

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012c. Guidance for the preparation of dossiers for zootechnical additives. EFSA Journal 2012;10(1):2536, 19 pp. doi:10.2903/j.efsa.2012.2536

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012d. Guidance for establishing the safety of additives for the consumer. EFSA Journal 2012;10(1):2537, 12 pp. doi:10.2903/j.efsa.2012.2537

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012e. Guidance on studies concerning the safety of use of the additive for users/workers. EFSA Journal 2012;10(1):2539, 5 pp. doi:10.2903/j.efsa.2012.2539

Gaynor PJ, Mueller FJ, Miller JK and Ramsey H, 1989. Parturient hypocalcemia in Jersey cows fed alfalfa haylage-based diets with different cation to anion ratios. Journal of Dairy Science 72: 2525-2531.

Gelfert CC, Engel M, Maenner K and Staufenbiel K, 2009. The effect of various anionic salts on ruminal pH and short-chain fatty acids in non-pregnant and non-lactating cows. New Zealand Veterinary Journal 57: 225-228.

Goff JP, Ruiz R and Horst RL, 2004. Relative acidifying activity of anionic salts commonly used to prevent milk fever. Journal of Dairy Science, 87:1245-1255.

Goff JP, 2008. The monitoring, prevention, and treatment of milk fever and subclinical hypocalcemia in dairy cows. The Veterinary Journal, 176:1, 50–57.

Horst RL, Jorgensen NA, 1974. Effect of ammonium chloride on nitrogen and mineral balance in lactating and nonlactating goats. Journal of Dairy Science, 57, 683–688.

Izquierdo JV and Czarnecki-Maulden GL, 1991. Effect of various agents on urine pH and acid-base balance in adult cats. Journal of Nutrition 121: S89-S90.

Jones ML, Streeter, RN and Goad, CL, 2009. Use of dietary cation anion difference for control of urolithiasis risk factors in goats. American Journal of Veterinary Research, 70, 149-155 Kienzle E and Wilms-Eilers S, 1994. Struvite diet in cats: Effect of ammonium chloride and carbonates on acid-base balance of cats. Journal of Nutrition 124: 2652S-2659S

Kienzle E and Wilms-Eilers S, 1994. Struvite diet in cats: effect of ammonium chloride and carbonates on acid base balance of cats. Journal of Nutrition, 124, 2652S–2659S.

Kienzle E, Thielen C and Janowicz P, 1998. Effect of urinary acidification using ammonium chloride on renal magnesium excretion in cats. Journal of Animal Physiology and Animal Nutrition 80: 130-133

Mellau LSB, Jurgensen RJ and Kambarage DM, 2002. The influence of short-term anion salt exposure on urine pH and on resistance to experimentally induced hypocalcaemia in cows. Journal of Veterinary Medicine Series A, 49:225-229.

Moore SJ, Vandehaar MJ, Sharma BK, Pilbeam TE, Beede DK, Bulcholtz HF, Liesman JS, Horst RL and Goff JP, 2000. Effects of altering dietary cation-anion difference on calcium and energy metabolism in peripartum cows. Journal of Dairy Science. 83: 2095-2104.

Oetzel GR, Olson JD, Curtis CR and Fettman MJ, 1988. Ammonium chloride and ammonium sulphate for prevention of parturient paresis in dairy cows. Journal of Dairy Science. 71: 3302-3309.

Oetzel GR, Fettman MJ, Hamar, DW and Olson JD, 1991. Screening of anionic salts for palatability, effects on acid-base status, and urinary calcium excretion in dairy cows. Journal of Dairy Science 74, 965-971.

Satter LD and Slyter LL, 1974. Effect of ammonia concentration of rumen microbial protein production in vitro. British Journal of Nutrition 32: 199-208.

Senior DF, Merchant SR and Sundstrom DA, 1984. Ammonium chloride as a long-term urinary acidifier in the dog. California Veterinarian 11: 7-9.

Shaw DH, 1989. Acute response of urine pH following ammonium chloride administration to dogs. American Journal of Veterinary Research 50; 1829-1830.

Suttle NF, 2010. Mineral Nutrition of Livestock, 4th ed. CAB International, Wallingford and Cambridge, p. 54-91.

Taton GF, Hamar DW and Lewis LD, 1984. Evaluation of ammonium chloride as a urinary acidifier in the cat. Journal of the American Veterinary Medical Association 184: 433-436.

Wang C and Beede DK, 1992. Effects of ammonium chloride and sulphate on acid-base status and calcium metabolism of dry dairy cows. Journal of Dairy Science 75: 820-828.

Abbreviations

CAS	Chemical Abstracts Service
DCAD	dietary cation anion difference
EC	European Commission
EINECS	European Inventory of Existing Commercial Chemical Substances
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
LOD	limit of detection
NPN	non-protein nitrogen